IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

IMPAX LABORATORIES, INC.,	:	
	:	
Plaintiff,	:	
	:	
v.	:	Civil Action No.
	:	02-581-JJF
AVENTIS PHARMACEUTICALS, INC.,	:	
	:	
Defendant.	:	

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MEMORANDUM OPINION

December 12, 2002
Wilmington, Delaware

FARNAN, District Judge

Presently before the Court is Defendant's Motion for Preliminary Injunction (D.I. 21). For the reasons set forth below, Defendant's Motion (D.I. 21) will be granted.

INTRODUCTION

Plaintiff Impax Laboratories, Inc. ("Impax") brought this declaratory judgment action seeking a judicial declaration of invalidity and non-infringement of U.S. Patent No. 5,527,814 ("the '814 patent"). The '814 patent, now owned by Defendant Aventis Pharmaceuticals, Inc. ("Aventis"), issued June 18, 1996, and is entitled "Use of 2-amino-6-(trifluoromethoxy)benzothiazole for Obtaining a Medicament for the Treatment of Amyotrophic Lateral Sclerosis." The '814 patent is directed to a method of treating Amyotrophic Lateral Sclerosis ("ALS"), commonly referred to as Lou Gehrig's Disease, by administering an effective dose of riluzole to a mammal in need of treatment. Aventis currently sells riluzole, for the treatment of ALS, under the trade name Rilutek®. Impax seeks to market a generic version of riluzole.

In May 2001, Impax filed an Abbreviated New Drug Application ("ANDA") with the Food and Drug Administration ("FDA") seeking approval to manufacture and sell 50 milligram tablets of riluzole to ALS patients. In its ANDA, Impax stated that its generic riluzole tablets are bioequivalent to Aventis's Rilutek® and asserted that it intended to enter the market promptly upon

receiving FDA approval. In July 2002, the FDA tentatively approved Impax's ANDA, and Impax has represented that it intends to enter the market when the orphan drug exclusivity for Rilutek® expires on December 12, 2002.[1] On October 15, 2002, Aventis brought this Motion for Preliminary Injunction (D.I. 21) to forestall Impax's entry into the riluzole market until the instant case can be resolved on the merits.

DISCUSSION

A party seeking a preliminary injunction pursuant to 35 U.S.C. § 283 must establish: "(1) a reasonable likelihood of success on the merits; (2) irreparable harm if an injunction is not granted; (3) a balance of hardships tipping in its favor; and (4) the injunction's favorable impact on the public interest." Amazon.com, Inc. v. Barnesandnoble.com, Inc., 239 F.3d 1343, 1350 (Fed. Cir. 2001). "These factors, taken individually, are not dispositive; rather, the district court must weigh and measure each factor against the other factors and against the form and magnitude of the relief requested." Hybritech, Inc. v. Abbott Labs., 849 F.2d 1446, 1451 (Fed. Cir. 1988).

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[1] Aventis, in its Opening Brief, asserts that the orphan drug exclusivity period for Rilutek® expires on December 17, 2002. (D.I. 22 at 9). Impax, in its Answering Brief, asserts that the exclusivity period ends on December 12, 2002. (D.I. 33 at 31). During the December 6, 2002, oral argument on the pending motion, counsel represented to the Court that the exclusivity period ends on December 12, 2002, and thus, the Court is using that date.

The Court will consider the relevant factors in *seriatim*.

1. Likelihood of Success on the Merits

With regard to the requirement of likelihood of success on the merits, the moving party must show, consistent with the burdens of proof required at trial, that (1) its patent was infringed, and (2) any challenges to the validity and enforceability of its patent "lack substantial merit." Purdue Pharma L.P. v. Boehringer Ingelheim GmbH, 237 F.3d 1359, 1366 (Fed. Cir. 2001). If the alleged infringer raises a substantial question concerning validity by asserting an invalidity defense that the patentee is unable to prove "lacks substantial merit," then the preliminary injunction will not issue. Genentech, Inc. v. Novo Nordisk, 108 F.3d 1361, 1364 (Fed. Cir. 1997); see also Novo Nordisk A/S v. Bio-Technology General Corp., No. 02-1447, 2002 WL 31684813, at *5 (Fed. Cir. Nov. 26, 2002)(unpublished). "Thus, the patent challenger retains the burden of establishing invalidity, and the applicant for preliminary injunctive relief retains the burden of showing a reasonable likelihood that the attack on the validity of the patent would fail." Robert L. Harmon, Patents and the Federal Circuit § 13.2(b)(5th ed. 2001).

Because Impax does not contest the facts concerning infringement (D.I. 22 at A48-A54), the Court finds, for purposes of this Motion only, that Impax's sale of generic riluzole would induce infringement of the '814 patent.

Impax contends that the '814 patent is invalid because it was anticipated by prior art.[2] An invention is anticipated under 35 U.S.C. § 102(b) if it "was ... described in a printed publication in this ... country ... more than one year prior to the date of application for patent in the United States." 35 U.S.C. § 102(b). "A rejection for anticipation under section 102 requires that each and every limitation of the claimed invention be disclosed in a single prior art reference." In re Paulsen, 30 F.3d 1475, 1478-79 (Fed. Cir. 1994)(citing In re Spada, 911 F.2d 705, 708 (Fed. Cir. 1990)); see also Scripps Clinic & Research Found. v. Genentech, Inc., 927 F.2d 1565, 1576 (Fed. Cir. 1991)("There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention.").

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[2] A determination of anticipation involves two steps. Harmon, supra, § 3.2(g). The first is to construe the claim, and the second is to compare the construed claim to the prior art. Id. In the instant case and for purposes of this Motion only, the Court finds that the claims of the '814 patent will be interpreted on the basis of their plain language because the meaning of the claim terms is clear and undisputed. See U.S. Surgical Corp. v. Ethicon, Inc., 103 F.3d 1554, 1568 (Fed. Cir. 1997)("Claim construction is a matter of resolution of disputed meanings and technical scope, to clarify and when necessary to explain what the patentee covered by the claims, for use in the determination of infringement. It is not an obligatory exercise in redundancy."); see also Sofamor Danek Group, Inc. v. DePuy-Motech, Inc., 74 F.3d 1216, 1221 (Fed. Cir. 1996)(noting that a trial court has no obligation to interpret claims conclusively and finally during a preliminary injunction proceeding). Thus, the Court will focus its analysis on the second step, i.e., comparing the claims of the '814 patent to the prior art.

To prevail, Impax has the burden of proving there is a substantial question concerning whether the '814 patent is anticipated by a single prior art reference that disclosed each and every limitation of the claimed invention. For Aventis to prevail it must prove that Impax's invalidity defense of anticipation lacks substantial merit.

The '814 patent includes 13 method claims directed to a treatment of ALS. Claims 1, 4, and 5 are illustrative:

> 1. A method for treating a mammal with amyotrophic lateral sclerosis, comprising the step of administering to said mammal in recognized need of said treatment an effective amount of 2-amino-6-(trifluoromethoxy)benzothiazole or a pharmaceutically acceptable salt thereof.
>
> 4. The method according to claim 1, wherein said effective amount comprises 25 to 200 mg of said 2-amino-6-(trifluoromethoxy)benzothiazole or said salt thereof.
>
> 5. The method according to claim 4, wherein said effective amount comprises 50 mg.

(D.I. 22 at A6).

Impax contends that claim 1 of the '814 patent is anticipated by U.S. Patent No. 4,826,860 ("the Johnson patent"). The Johnson patent states that:

> The instant invention concerns a new method for treating cerebrovascular disorder, such disorders are those in which excitatory amino acids, for example, glutamatic [*sic*, glutamic] and aspartic acids, are implicated. Such disorders include cerebral ischemia or cerebral infarction resulting from a range of conditions such as thromboembolic or hemorrhagic stroke, cerebral vasospasm, hypoglycemia, cardiac arrest, status epilepticus, or cerebral trauma. Other

> treatments are for schizophrenia, epilepsy, neuromuscular disorders, Alzheimer's Disease, or Huntington's Disease.
> ...
> This method of treatment comprises administering a therapeutically effective amount of a compound.... The more preferred compounds are: ... 2-amino-6-trifluoromethoxybenzothiazole....

(D.I. 33 at B150-51).

Impax contends that the Johnson patent discloses a method for treating a mammal with neuromuscular disorders in which excitatory amino acids, such as glutamic and aspartic acids, are implicated. Impax further contends, based the declaration of its expert, Theodore L. Munsat, M.D. (D.I. 33 at B4-13), that because ALS is the only neuromuscular disorder in which excitatory amino acids are implicated, the term "neuromuscular disorders" in the Johnson patent is understood by those skilled in the art to mean ALS. Additionally, since the Johnson patent specifically discloses the use of riluzole to treat neuromuscular disorders, Impax contends the Johnson patent discloses each and every element of claim 1 of the '814 patent.

Aventis contends there are three reasons why Impax's argument that the term "neuromuscular disorders" in the Johnson patent should be understood by one of ordinary skill in the art to mean ALS is flawed: (1) the plain language of the passage on which Impax relies is inconsistent with Impax's position; (2) Impax's arguments concerning the implication of glutamate in ALS are misleading and rely on impermissible hindsight; and (3) the

specification and claims of the Johnson Patent directly contradict Impax's argument.

Considering the evidence offered by Impax and Aventis on the meaning of the term "neuromuscular disorders, the Court finds that Aventis's expert, Benjamin Rix Brooks, M.D., is more credible than Impax's expert, Dr. Munsat. To begin with, Dr. Munsat has expressed contrary opinions. Specifically, Dr. Munsat offered an opinion during the prosecution of the '814 patent different from his present opinion. During the prosecution, Dr. Munsat opined that "in March 1992, one skilled in the art ... would have had no reasonable expectation that Riluzole would be successful in treating ALS," (D.I. 22 at A23) but now, he contends that "the Johnson patent [which issued on May 2, 1989] discloses a method for the treatment of a human with amotrophic lateral sclerosis by administering 2-amino-6-trifluoromethocybenzothiazole [riluzole]." (D.I. 33 at B5).

On the other hand, Dr. Brooks has unequivocally opined that he finds "no basis to conclude that the Johnson patent meant 'neuromuscular disorders' to mean only ALS." (D.I. 40 at C50). Based on the opinion of Dr. Brooks and the reasons he offers in suport of his opinion, the Court concludes that Impax has not raised a substantial question as to whether the Johnson patent

anticipates claim 1 of the '814 patent.[3] Therefore, the Court concludes that for purposes of the present motion the term "neuromuscular disorders" as used in the Johnson patent is not understood by one of ordinary skill in the art to mean ALS and ALS alone. The Court interprets the term "neuromuscular disorders" to be a plural term that refers to a broad category of disorders.

Furthermore, the Court concludes, based on the declaration of Dr. Brooks,[4] that the syntax of the paragraph relied on by Impax for its contention that because ALS is the only neuromuscular disorder in which excitatory amino acids are implicated, the term "neuromuscular disorders" in the Johnson patent means ALS does not support Impax's argument. The first sentence of the paragraph discloses a method of treating cerebrovascular disorders in which excitatory amino acids are implicated; the second sentence lists and/or describes particular cerebrovascular disorders in which excitatory amino acids are implicated; and the third sentence lists other disorders,

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[3] Since the Court concludes that the Johnson patent does not anticipate claim 1 of the '814 patent, and claims 4 and 5 are dependent on and narrower then claim 1, the Court also concludes that the Johnson patent does not anticipate claims 4 and 5 of the '814 patent.

[4] Dr. Brooks explained that, "[t]he plain reading of the patent does not relate the term 'neuromuscular disorders' to 'excitatory amino acids....' The references are clearly set apart in different sentences where only the first sentence relates to glutamic acid." (D.I. 40 at C49-C50).

including neuromuscular disorders, that may be treated by the same method disclosed in the patent. The Court concludes that the syntactical structure of the paragraph indicates no relationship between excitatory amino acids and neuromuscular disorders; the former does not restrict the latter. Therefore, the Court concludes that one of ordinary skill in the art would have no basis upon which to conclude that the only neuromuscular disorders being referred to in the Johnson patent are those which implicate excitatory amino acids.

However, even if the Johnson patent discloses a method of treating neuromuscular disorders in which excitatory amino acids are implicated, the Court concludes that one of ordinary skill in the art would not conclude that the use of the term "neuromuscular disorders" refers only to ALS because at the time of the invention it was not clear that excitatory amino acids were implicated in ALS. Dr. Brooks' Declaration supports this conclusion:

> I have read where Impax and Dr. Munsat have taken the position that prior to 1992, excitatoxicity and particularly glutamate excitatoxicity were implicated with ALS. While it is true that some people theorized that glutamate activity may be related to ALS, in the 1992 time frame it was not a theory that was fully adopted by the profession. Indeed at that time there was significant resistance to the idea and it was very controversial.

(D.I. 40 at C49).

Additionally, in Young, What's the Excitement about Excitatory

Amino Acids in Amyotrophic Lateral Sclerosis?, Ann. Neurol., 28:9-11 (1990), a source originally cited by Dr. Munsat, the author states that "[i]t appears that although the hypothesis is intriguing, considerably more information needs to be gathered prior to concluding that excitatory amino acids play a role in ALS," and that "the hypothesis that excitatory amino acids play a role in the pathogenesis of ALS remains speculative." (D.I. 40 at C25). Since the link between excitatory amino acids and ALS was "controversial" and "speculative," the Court concludes that one of ordinary skill in the art would not have concluded that ALS was the neuromuscular disorder described in the Johnson patent.

In sum, the Court concludes, as to the Johnson patent assertion, Impax has not raised a substantial question as to the validity of the '814 patent. Also, the Court concludes that the Johnson patent does not disclose a method of treating ALS, which is an element of the invention claimed in the '814 patent, and finally, the Court concludes that Aventis has demonstrated that Impax's anticipation defense lacks substantial merit.

Impax also contends that the '814 patent is anticipated by a paper written by Edith McGreer, entitled Excitatory Amino Acid Neurotransmission and its Disorders ("the McGreer paper," D.I. 40 at C31-C37). Specifically, Impax contends that the McGreer paper discloses to one of ordinary skill in the art that riluzole can

protect against the neuronal degeneration associated with ALS by inhibiting EAA release.

In response, Aventis contends that the McGreer paper does not state that riluzole treats ALS. Aventis asserts that the McGreer paper refers to riluzole in only one diagram with no elaboration or discussion, and therefore, the McGreer paper does not disclose each element of claim 1 of the '814 patent.

The Court concludes, based on the Declaration of Dr. Brooks which states that the McGreer article does not teach the use of riluzole to treat ALS (D.I. 40 at C50), that Impax has not raised a substantial question as to whether the McGreer paper anticipates the '814 patent. Also, the Court concludes that Aventis has demonstrated that Impax's anticipation defense based on the McGreer paper lacks substantial merit.

After reviewing the contentions of the parties (including those not directly addressed above), the relevant facts, and the applicable law, the Court concludes that Aventis has shown that Impax's anticipation defenses lack substantial merit.

2. Irreparable harm

Irreparable harm is presumed when a clear showing of patent validity and infringement has been made. Amazon.com, Inc., 239 F.3d at 1350 (citing Bell & Howell Document Mgmt. Prods. Co. v. Altek Sys., 132 F.3d 701, 708 (Fed. Cir. 1997). "This presumption derives in part from the finite term of the patent

grant, for patent expiration is not suspended during litigation, and the passage of time can work irremediable harm." Id.

Here, Aventis has made a clear showing of infringement and validity, and thus, for purposes of this analysis, the Court presumes that not granting the preliminary injunction would cause Aventis irreparable harm.

3. Balance of Hardships

Important considerations in weighing the balance of hardship include, but are not limited to, whether the hardship to the alleged infringer would be merely temporary in duration, and whether the infringer had yet entered the market. Ortho Pharm. Corp. v. Smith, 15 U.S.P.Q. 2d 1856 (E.D. Pa. 1990).

Aventis contends that granting the Motion for Preliminary Injunction will create only minimal hardship for Impax but would cause substantial hardship for Aventis. Aventis points out that Impax has not entered the market and would only be delayed in doing so for the duration of this litigation, which is scheduled for trial in October 2003. In contrast, Aventis contends it has invested substantial time and money developing Rilutek® and would lose the ability to recoup its costs if Impax is allowed to prematurely enter the market with a generic product.

Impax contends that the Aventis' research and development costs for Rilutek® were fairly modest and that the Orphan Drug Act has already provided Aventis sufficient time to recoup its

costs.

The Court finds that granting the Motion for Preliminary Injunction will cause Impax only minimal hardship since doing so will leave Impax in the same position as it was in before the injunction was granted, i.e., excluded from the riluzole market. The Court also finds that allowing Impax to prematurely enter the riluzole market with a generic product would cause substantial financial hardship to Aventis. Additionally, the Court finds that the October 2003 trial date mitigates any hardship to Impax and weighs in favor of granting the preliminary injunction. For these reasons, the Court concludes that the balance of hardship tips in Aventis' favor.

4. Public interest

"The public has an interest in the enforcement of valid patents." Corning Glass Works v. Sumitomo Electric U.S.A., Inc., 132 F. Supp. 2d 365 (S.D.N.Y. 1987). "Typically, in a patent infringement case, although there exists a public interest in protecting rights secured by valid patents, the focus of the district court's public interest analysis should be whether there exists some critical public interest that would be injured by the grant of preliminary relief." Hybritech Inc. v. Abbott Laboratories, 849 F.2d 1446, 1458 (Fed. Cir. 1988)(footnotes omitted)(finding the public interest in enforcing valid patents outweighed the adverse impact on the market caused by the alleged

infringer's absence).

Aventis contends that no public interest will be adversely affected by granting the preliminary injunction and that denying the injunction will adversely impact the public's interest in protecting intellectual property rights.

Impax contends that granting the preliminary injunction will adversely impact the public interest in obtaining cheaper generic forms of drugs. Moreover, Impax contends that denying the preliminary injunction would support the public interest in compelling companies like Aventis to obey the provisions of 21 U.S.C. § 355. Impax argues that if Aventis had complied with Section 355, it would have automatically received the delay it now seeks through a preliminary injunction, and therefore, Aventis should not be rewarded for not complying with federal law.

The Court finds that the public interest in protecting valid patent rights is not outweighed by any competing public interests. Specifically, the Court finds that granting the preliminary injunction comports with the public interest as expressed by Congress in 21 U.S.C. § 355. But for Aventis' noncompliance with Section 355, Impax would have been prevented from entering the riluzole market for thirty months because Congress thought it was in the public interest to have the judicial system determine issues of infringement and validity

before manufacturers of patented pharmaceuticals were exposed to lower priced competition from generic drug makers. See 21 U.S.C. § 355(j)(5)(B)(iii). Thus, the Court concludes that there is a strong public interest in protecting valid patents by preventing the premature entry of generic drugs into the marketplace. For these reasons, the Court concludes that granting a preliminary injunction in the instant case will have a favorable impact on the public interest.

CONCLUSION

For the reasons discussed, Aventis' Motion for Preliminary Injunction (D.I. 21) will be granted.

The Parties shall confer and submit a proposed Order to the Court no later than Friday, December 13, 2002, at 3:00 p.m.